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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,710	04/08/2004	Michael Wayne Graham	0763/74768-BAA-PCT-US/JPW	1697

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	
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04/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,710	GRAHAM ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44,77-100,102,104-113 and 142-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44,77-100,102,104-113 and 142-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/646,807.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/26/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 2/11/08.

Claims 142-144 were added.

Claims 44, 77-100, 102, 104-113, and 142-144 are pending and are under consideration.

Rejections not reiterated are withdrawn.

Information Disclosure Statement

The information disclosure statement filed 2/29/08 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the inventors or Applicants are not named for each one of the cited US Patent documents. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

The information disclosure statement filed 2/29/08 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the cited references were not received. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of

any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Priority

At page 23 of the response, Applicant argues that the first effective filing date of the instant application is 3/20/1998. this corresponds to the filing dates of Australian Provisional Patent Applications PP2492, and PP2499. However, the Examiner did not find support in either PP2492 nor PP2499 for a first ribonucleotide sequence of greater than 20 consecutive nucleotides that is identical in sequence to a region of a transcript of any target gene in a eukaryotic cell, as recited in instant claim 44. Support for independent claim 44 as amended on 11/20/06 can be found in PCT/AU99/00195, filed 3/19/99. Thus the instant claims cannot have an effective filing date earlier than 3/19/99. If Applicant feels that this is not the case, then Applicant is invited to point to specific support in the priority documents by page and line number.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 144 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 144 is indefinite because it is unclear what is meant by greater than 20-100 consecutive nucleotides. For example, 80 nucleotides is greater than 20 nucleotides, but not greater than 100 nucleotides, so it is unclear if 80 nucleotides is embraced by the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44, 77, 80-87, 90, 91, 97, 98, 104-106, 110, 111, and 144 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al (WO 94/01550, of record).

Agrawal taught self-stabilizing RNA molecules comprising a region that is complementary to a target in a eukaryotic mRNA in a human cell and a region that is self-complementary. See abstract; page 8, lines 7-11 and 22-24, paragraph bridging pages 11 and 12, and page 13, lines 25-30. The target hybridizing region is from 8 to

50 nucleotides in length (sentence bridging pages 9 and 10). The size of the self complementary region may vary, but may be so extensive as to involve every nucleotide of the oligonucleotide, i.e. it may be 8-50 nucleotides in length (see page 15, lines 3-6, 16-21, and 26-30. The resulting RNA may form a hairpin structure comprising a loop, see page 15, lines 12-16, and Fig. 1. The loop is considered to be a "stuffer" sequence. Thus Agrawal fairly taught a double stranded RNA comprising a target hybridizing region of 8-50 ribonucleotides, a loop, and a self-complementary region of 8-50 nucleotides.

The target gene may be a viral gene. Disclosed viruses include human immunodeficiency virus, Yellow Fever virus (a single strand (+) RNA virus), and Herpes simplex virus (a double stranded DNA virus). See paragraph bridging pages 10 and 11. The target may be a member of a multi-gene family such as ras. See page 12, line 10. The oligonucleotide may be in a pharmaceutically acceptable carrier. See page 18, lines 5-8 and claim 18. Absent evidence of unexpected results, it would have been obvious to one of ordinary skill in the art to vary the length of the unpaired loop sequence of the self-stabilizing RNA of Agrawal in order to optimize hybridization of the complementary section of the oligonucleotides, thereby providing increased stability against nucleolytic attack.

Claims 44, 77, 80-82, 85-95, 97-99, 102, 104-106, 108-113, and 142-144 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire (US 6,506,559

Fire disclosed and claimed methods for regulating gene expression in cells, including plant and animal cells, comprising introducing into a cell a double stranded RNA comprising a sequence complementary to a portion of the target gene and a sequence identical to a portion of the target gene. At column 4, lines 41-46 Fire et al. teach that the dsRNA can be formed from 2 strands, or from only a single self-complementary RNA strand, i.e. a hairpin construct. (See provisional application 60/068,562 at page 6, lines 17-22). At columns 7-9, Fire taught that the RNA can be synthesized in vivo or in vitro, and can be expressed from a vector, and can have a length of greater than 25, 50, 100, 200, 300, or 400 nucleotides (see col. 7, line 53 to col. 8, line 12; or provisional application at page 12, lines).

Thus Fire fairly taught self-complementary RNA strands of greater than 400 bases in, e.g. 25 consecutive nucleotides were identical to a sequence of a region of a target mRNA sequence, and another 25 consecutive nucleotides were complementary to that target sequence. In such a molecule, an arbitrary number of nucleotides associated with the inherent hairpin region of the RNA strand can be arbitrarily considered to be a stuffer fragment that links 25 complementary base pairs This molecule could have a stuffer regions of 10, 50, or 100 nucleotides based on the arbitrary designation of what is, and what is not, the stuffer sequence.

Fire also taught that the target gene can be a transgene (column 6, lines 44-49), a multigene family member (column 1, lines 13-16), a dicot (bean) or monocot (corn) plant gene (column 8, lines 14, 15, 20 and 21), a vertebrate, invertebrate, fish,

mammal, human, or insect gene (column 8, lines 35-51), and can be delivered by a virus (column 9, lines 56-59, provisional at page 12, lines 8-12).

Thus Fire anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 44, 77-91, 97, 98, 104-106, 110-113, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 94/01550, of record) in view of Day et al (Proc. Nat Acad. Sci. USA 88: 6721-6725, 1991).

Agrawal taught self-stabilizing RNA molecules comprising a region that is complementary to a target in a eukaryotic mRNA in a human cell and a region that is self-complementary. See abstract; page 8, lines 7-11 and 22-24, paragraph bridging pages 11 and 12, and page 13, lines 25-30. The target hybridizing region is from 8 to 50 nucleotides in length (sentence bridging pages 9 and 10). The size of the self complementary region may vary, but may be so extensive as to involve every nucleotide of the oligonucleotide, i.e. it may be 8-50 nucleotides in length (see page 15, lines 3-6, 16-21, and 26-30. The resulting RNA may form a hairpin structure comprising a loop, see page 15, lines 12-16, and Fig. 1. The loop is considered to be a “stuffer” sequence. Thus Agrawal fairly taught a double stranded RNA comprising a target hybridizing

region of 8-50 ribonucleotides, a stuffer fragment, and a self-complementary region of 8-50 nucleotides.

The target gene may be a viral gene. Disclosed viruses include human immunodeficiency virus, Yellow Fever virus (a single strand (+) RNA virus), and Herpes simplex virus (a double stranded DNA virus). See paragraph bridging pages 10 and 11. The target may be a member of a multi-gene family such as ras. See page 12, line 10. The oligonucleotide may be in a pharmaceutically acceptable carrier. See claim 18. Absent evidence of unexpected results, it would have been obvious to one of ordinary skill in the art to vary the length of the unpaired loop sequence of the self-stabilizing RNA of Agrawal in order to optimize hybridization of the complementary section of the oligonucleotides, thereby providing increased stability against nucleolytic attack.

Agrawal did not teach RNA molecules directed against a plant virus, or an expression construct encoding the RNA molecules.

Day taught that transgenic plants comprising an expression construct encoding antisense RNA directed against a Gemini virus gene were resistant to the virus. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Day by designing an expression construct encoding a self-stabilizing RNA molecule as taught by Agrawal. One would have been motivated to do so in order to increase the stability of the antisense RNA, thereby providing a reasonable expectation of improving viral resistance.

Thus the invention as a whole was prima facie obvious.

Claims 44, 77, 80-87, 90, 91, 97-99, 104-113, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 94/01550, of record) in view of Kool (US 5,514,546).

The teachings of Agrawal are discussed above, and anticipate double stranded RNAs comprising a target hybridizing region of 8-50 ribonucleotides, a loop, and a self-complementary region of 8-50 nucleotides, wherein the target is e.g. a viral gene, or a mammalian multi-family gene.

Agrawal did not explicitly teach vectors encoding the antisense oligonucleotides, oligonucleotides targeting a coding region, or liposome-containing compositions.

Kool taught delivery of stem-loop oligonucleotides by expression vector or by direct application of the oligonucleotides. See abstract; Fig. 1; column 3, lines 16-19 and lines 58-62; column 4, lines 6-17; and column 14, lines 39-. Kool also disclosed antisense inhibition by targeting coding regions. See column 7, lines 43-46. Kool also disclosed delivery of expression vectors by viral- or liposome-mediated transfection. See column 15, lines 36-45; column 16, lines 43-47; paragraph bridging columns 24 and 25; and column 29, lines 32 and 33.

It would have been obvious to one of ordinary skill in the art at the time of the invention to deliver the oligonucleotides of Agrawal by use of the expression vector of Kool. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one

equivalent component or process for another is not necessary to render such substitution obvious. Thus the delivery techniques of Kool, i.e. direct application of oligonucleotides, and transfection of oligonucleotide expression vectors, are considered to be exchangeable equivalents. Alternatively, the method of delivering the oligonucleotides can be viewed as a matter of design choice. Moreover, one would have been motivated to use the expression vector of Kool in order to obtain continuous synthesis and action of oligonucleotides for the amount of time that the vector was present in the cell. Generally, expression vectors can be made with selectable markers that allow their maintenance in a cell for a longer time than the expected lifetime of an oligonucleotide. Thus one could reasonably expect to obtain antisense inhibition for a longer period of time with the expression vector of Kool.

It would have been similarly obvious to target coding regions of target genes, and to deliver the vectors by viral or liposomal means as suggested by Kool.

Thus the invention as a whole was prima facie obvious.

Claims 44, 77, 80-87, 90-92, 94, 97, 98, 104-106, 110, 111, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 94/01550, of record) in view of McGarry et al (Proc Nat. Acad. Sci. USA 83:399-403, 1986).

Agrawal taught self-stabilizing RNA molecules comprising a region that is complementary to a target in a eukaryotic mRNA in a human cell and a region that is self-complementary. See abstract; page 8, lines 7-11 and 22-24, paragraph bridging pages 11 and 12, and page 13, lines 25-30. The target hybridizing region is from 8 to

50 nucleotides in length (sentence bridging pages 9 and 10). The self complementary regions may be separated by an unpaired loop structure (see e.g. Fig. 1, and page 15, lines 9-16).

Agrawal did not teach RNA molecules comprising an intron, or RNA molecules directed against an RNA in a cell of an invertebrate animal or insect.

McGarry taught methods of inhibiting gene expression by expression of antisense RNA in cultured Drosophila cells.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of McGarry by designing an expression construct encoding a self-stabilizing RNA molecule as taught by Agrawal. One would have been motivated to do so in order to increase the stability of the antisense RNA, thereby providing a reasonable expectation of improving antisense performance.

Buchman taught that the inclusion of an intron in an expression construct could stimulate transcription of the expressed by 400-fold. See abstract,.

It would have been obvious to include an intron in the expression vector of McGarry in order to obtain the benefit of increased expression as taught by Buchman. The resulting transcripts would contain, prior to processing, an intron.

Thus the invention as a whole was prima facie obvious.

Claims 44, 77, 80-87, 90, 91, 93, 95, 97, 98, 104-106, 110, 111, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 94/01550, of record) in view of Barabino et al (Mech. Dev. 63: 133-143, 1997).

Agrawal taught self-stabilizing RNA molecules comprising a region that is complementary to a target in a eukaryotic mRNA in a human cell and a region that is self-complementary. See abstract; page 8, lines 7-11 and 22-24, paragraph bridging pages 11 and 12, and page 13, lines 25-30. The target hybridizing region is from 8 to 50 nucleotides in length (sentence bridging pages 9 and 10). The self complementary regions may be separated by an unpaired loop structure (see e.g. Fig. 1, and page 15, lines 9-16).

Agrawal did not teach RNA molecules directed against an RNA in a cell of an aquatic animal.

Barabino taught methods of suppressing Alx gene expression in zebrafish embryos by administration of antisense oligonucleotides. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Barabino by designing and using expression vectors encoding self-stabilizing antisense RNA molecules as taught by Agrawal. One would have been motivated to do so in order to increase antisense performance.

Thus the invention as a whole was prima facie obvious.

Claims 44, 77, 80-87, 90, 91, 96-98, 104-106, 110, 111, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 94/01550, of record) in view of Swamynathan et al (J. Virol. 71(4): 2873-2880, 1997).

Agrawal taught self-stabilizing RNA molecules comprising a region that is complementary to a target in a eukaryotic mRNA in a human cell and a region that is

self-complementary. See abstract; page 8, lines 7-11 and 22-24, paragraph bridging pages 11 and 12, and page 13, lines 25-30. The target hybridizing region is from 8 to 50 nucleotides in length (sentence bridging pages 9 and 10). The self complementary regions may be separated by an unpaired loop structure (see e.g. Fig. 1, and page 15, lines 9-16).

Agrawal did not teach RNA molecules directed against an RNA in a cell of an avian animal.

Swamynathan taught a method of inhibiting expression of chicken YB-2 in avian fibroblasts by administration of antisense RNA directed against the ama-1 gene. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Swamynathan by designing and using self-stabilizing antisense RNA molecules as taught by Agrawal. One would have been motivated to do so in order to increase antisense performance.

Thus the invention as a whole was prima facie obvious.

Claims 44, 77, 80-91, 97-100, 104-106, 110-113, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al (WO 94/01550, of record) in view of Shewmaker et al (US Patent 5,107,065.

Agrawal taught self-stabilizing RNA molecules comprising a region that is complementary to a target in a eukaryotic mRNA in a human cell and a region that is self-complementary. See abstract; page 8, lines 7-11 and 22-24, paragraph bridging

pages 11 and 12, and page 13, lines 25-30. The target hybridizing region is from 8 to 50 nucleotides in length (sentence bridging pages 9 and 10). The self complementary regions may be separated by an unpaired loop structure (see e.g. Fig. 1, and page 15, lines 9-16).

Agrawal did not specifically teach an RNA with sequence identical to a region of a transcript in a plant cell, but noted that antisense regulation of gene expression in plant cells had been described, by Shewmaker, incorporating the teachings of Shewmaker by reference. Agrawal did not specify that the targeted region of the transcript was in the coding region or the 5'- or 3'-untranslated regions of the target. Agrawal did not teach an expression construct encoding the RNA molecules.

Shewmaker taught antisense regulation of gene expression in monocot or dicot plant cells by integrating into the genome of the plant cell a construct comprising in the 5'-3' direction of transcription a promoter functional in said plant cell, a dsDNA sequence wherein the transcribed strand of said dsDNA is complementary to RNA indigenous to said cell, whereby said complementary strand is transcribed and binds to said RNA indigenous to said cell, thereby inhibiting expression of said gene indigenous to said plant cell. See abstract, column 4, lines 1-3, and claims 6 and 7. The transcribed RNA can comprise sequence from either the 5' or 3' untranslated region. See e.g. claims 3 and 4. Alternatively the transcribed RNA can comprise sequence from all or part of the coding region. See column 2, lines 33-50.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Shewmaker by designing an expression construct

encoding a self-stabilizing RNA molecule as taught by Agrawal. One would have been motivated to do so in order to increase the stability of the antisense RNA, thereby providing a reasonable expectation of improving antisense performance.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 2/11/08 have been considered as they might apply to the new grounds of rejection above but they are not persuasive.

Applicant argues at page 15 of the response that Agrawal does not disclose: 1) "a first RNA sequence of greater than 20 consecutive nucleotides which is identical in sequence to a region of a transcript of a target gene", 2) "a second RNA sequence of greater than 20 consecutive nucleotides which is identical to a complement of the greater than 20 consecutive nucleotides of said first RNA sequence" or 3) "separated and linked by a stuffer fragment", as recited in claim 44.

This is incorrect. Agrawal clearly indicates that the target hybridizing region is from 8 to 50 nucleotides in length (sentence bridging pages 9 and 10), the self complementary region may range from a few base pairs up to every nucleotide of the oligonucleotide, i.e. it may be 8-50 nucleotides in length (see page 15, lines 3-6, 16-21, and 26-30. The resulting RNA may form a hairpin structure comprising a loop, see page 15, lines 12-16, and Fig. 1. The loop is the equivalent of the claimed stuffer.

Applicant indicates that Fig. 1 does not meet the limitations of the claims. This is unpersuasive because the teachings of Agrawal are not limited to Fig. 1. The entire reference must be considered for what it fairly teaches. Relevant portions of Agrawal are pointed out above and in the rejection.

Applicant argues at page 16 that Agrawal does not disclose or suggest how much of the self-complementary region complements the target hybridizing region, and points to passages in which Agrawal indicates that every nucleotide can be involved but about 10 base pairs is preferred. This is unpersuasive, the teachings of the reference are not limited to preferred embodiments. Agrawal fairly taught that up to 50 nucleotides of the targeting region could be paired by the self-complementary region. See above.

Applicant argues at page 16 that the oligonucleotides of Agrawal are described as necessarily activating RNase H, and so must comprise at least some DNA. Applicant refers to page 5, lines 9-12 and page 6, lines 1 and 2 or Agrawal. This is unpersuasive. Applicant's attention is directed to page 14 lines 8-10 which clearly state that "other embodiments employing target hybridizing regions that do not activate RNase H can also be made." One of ordinary skill at the time of the invention would have appreciated that RNA molecules could act by steric inhibition of translation, such that RNase H activity is not required. See also page 8, lines 7-11 which indicate that the molecules of Agrawal may consist of ribonucleotides and/or deoxyribonucleotides.

To the extent that Applicant's arguments at pages 18-21 might be applicable to the instant rejections, they are unpersuasive for the reasons set forth above. Allegations that the references cannot be combined are not supported.

Regarding the Fire reference, Applicant argues at page 23 of the response that Fire is not available as prior art. This is not persuasive for the reasons set forth above under Priority, i.e. priority documents PP2492 nor PP2499 do not provide support for a first ribonucleotide sequence of greater than 20 consecutive nucleotides that is identical in sequence to a region of a transcript of any target gene in a eukaryotic cell, as recited in instant claim 44. The effective filing date of the instant claims is 3/19/99, the filing date of PCT/AU99/00195.

Applicant's arguments at pages 24-25 of the response are based on the teachings of the Fire provisional application 60/068,562, and are unpersuasive because the Fire patent is available as prior art.

Applicant argues at page 24 that Fire does not teach 1) "a second RNA sequence of greater than 20 consecutive nucleotides which is identical to a complement of the greater than 20 consecutive nucleotides of said first RNA sequence", 2) "first and second RNA sequences of nucleotides are in the same nucleic acid" and 3) "separated by a stuffer fragment." This is unpersuasive. The term "stuffer fragment" is not defined in the instant specification, so it is given its broadest reasonable interpretation, which is single a segment of nucleic acid separating two other segments of nucleic acid. Fire taught self-complementary RNA strands of greater than 400 bases in, e.g. 25 consecutive nucleotides were identical to a sequence of a region of a target

mRNA sequence, and another 25 consecutive nucleotides were complementary to that target sequence. In such a molecule, any number of nucleotides associated with the inherent hairpin region of the RNA strand can be arbitrarily considered to be a stuffer fragment that links 25 complementary base pairs This molecule could have a stuffer regions of 10, 50, or 100 nucleotides based on the arbitrary designation of what is, and what is not, the stuffer sequence. See the rejection above.

For these reasons the rejections are considered proper.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Richard Schnizer, Ph. D./
Primary Examiner, Art Unit 1635